Jessy S Deshane et al., J Clin Cell Immunol 2016, 7:3(Suppl)
http://dx.doi.org/10.4172/2155-9899.C1.027

Suppression of B lymphopoiesis by myeloid-derived suppressor cells in tumor-bearing mice

Jessy S Deshane, Yong Wang, Cara C Schafer, Kenneth P Hough, John F Kearney and **Hui-Chen Hsu**
University of Alabama at Birmingham, USA

Rationale: Myeloid-derived suppressor cells (MDSCs) have been well established as regulators of anti-tumor immunity. MDSCs modulate amino acid metabolism in the tumor microenvironment and suppress T-cell function. However, it is less clear whether MDSCs regulate B-cell responses during tumor progression.

Methods: Using a syngeneic orthotopic model for lung cancer with murine Lewis Lung Carcinoma cells, we evaluated B-cell subsets in tumor bearing mice by multi parameter flow cytometry. The amount of serum IgG or IL-7 was determined by ELSIA. Phospho-STAT5 and total STAT5 were detected by immunoblotting. To investigate MDSC-mediated suppression of B cell lymphopoiesis, we adoptively transferred MDSCs derived from bone marrow of $CD45.2^+$ tumor bearing mice intratibially into congenic $CD45.1^+$ mice. B-cell subsets in recipient mice at day 7 post MDSC transfer were enumerated as above. *In vitro* B-cell inhibitory assay was performed by co-culturing CFSE-labeled pre-activated splenocytes with MDSCs purified from bone marrow of tumor-bearing mice at a ratio of 1:1 in the absence or presence of arginase inhibitor nor-NOHA (20 μM), iNOS inhibitor 1400W (500 nM) or IDO inhibitor 1-D-MT (1 mM) for 48 hours. The percentage of $CD19^+CFSE^{low}$ cells (proliferating cells) was determined by FACS analysis.

Results: Percentages and absolute numbers of Pro-, Pre- and mature B-cells were reduced in bone marrow (BM) of tumor bearing mice. Moreover, percentage and absolute number of follicular B cells were reduced, while immature B-cells increased in the spleen of tumor bearing mice. Levels of serum IgG were reduced in tumor-bearing mice. Furthermore, IL-7 and downstream STAT-5 signaling were impaired in tumor bearing mice. Transfer of BM-derived MDSCs from tumor bearing mice into congenic recipients resulted in significant reduction in both percentages and absolute numbers of immature and mature B-cells in peripheral blood of recipient mice. Pre-B cells and immature B-cells also decreased in BM of MDSC transferred recipients. Additionally, MDSCs suppress B-cell proliferation and IgG production by B-cells in an arginase and iNOS dependent but IDO independent manner.

Conclusions: In the present study, we demonstrate that B-cell differentiation *in vivo* is impaired in the BM and spleen of mice with lung cancer. Adoptive transfer studies with congenic mice demonstrate that MDSCs derived from Lewis Lung Carcinoma bearing mice may suppress B-cell differentiation in tumor naive mice. These results together suggest that tumor-related MDSCs may potentially regulate humoral immune responses to promote tumor survival.

Biography

Jessy S Deshane is a pulmonary Immunologist with expertise in immune regulation in asthma. She investigates myeloid-derived regulatory cell biology and free radical mechanisms that regulate their differentiation and function. She pioneered these investigations both in mouse models and human asthma. She has authored 46 peer-reviewed publications, including high impact journals like *Journal of Experimental Medicine, Journal of Clinical Investigations, Journal of Allergy* and *Clinical Immunology, Immunity* and *Cancer Research.* She serves on the Editorial Boards for the journals *Allergy* and *American Journal of Respiratory Cell* and *Molecular Biology* and serves on grant review committees.